

Prevention of cardiac hypertrophy in mice by calcineurin inhibition.

Sussman M A; Lim H W; Gude N; Taigen T; Olson E N; Robbins J; Colbert M C
; Gualberto A; Wieczorek D F; Molkentin J D

Division of Molecular Cardiovascular Biology, Children's Hospital Medical
Center, 3333 Burnet Avenue, Cincinnati, OH 45229, USA.

Science (UNITED STATES) Sep 11 1998 , 281 (5383) p1690-3, ISSN
0036-8075 Journal Code: 0404511

Contract/Grant No.: HL58224-01; HL; NHLBI

Publishing Model Print; Comment in Science. 1998 Nov 6;282(5391) 1007

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Hypertrophic **cardiomyopathy** (HCM) is an inherited form of heart disease that affects 1 in 500 individuals. Here it is shown that calcineurin, a calcium-regulated phosphatase, plays a critical role in the pathogenesis of HCM. **Administration** of the calcineurin inhibitors **cyclosporin** and FK506 prevented disease in mice that were genetically predisposed to develop HCM as a result of aberrant expression of tropomodulin, myosin light chain-2, or fetal beta-tropomyosin in the heart. **Cyclosporin** had a similar effect in a rat model of pressure-overload hypertrophy. These results suggest that calcineurin inhibitors merit investigation as potential therapeutics for certain forms of human heart disease.

Long-term follow-up and complications after cardiac transplantation.

Conrad S A; Chhabra A; Vay D

Willis Knighton-LSU Medical Center Heart and Lung Transplantation Center
in Shreveport.

Journal of the Louisiana State Medical Society - official organ of the
Louisiana State Medical Society (UNITED STATES) May 1993 , 145 (5)
p217-20, 223-5, ISSN 0024-6921 Journal Code: 7505618

Publishing Model Print

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Cardiac transplantation has become an established therapy for **cardiomyopathy** and other irreversible cardiac diseases. Improvements in immunosuppression and management of infections has improved long-term survival following transplantation. The role of the primary care physician in the care of recipients will be expanding. Transplant recipients receive close outpatient follow-up after discharge, primarily to monitor immunosuppression through laboratory evaluation and drug levels, monitor for rejection through endomyocardial biopsy, and to assess for any signs of opportunistic infection. The foundation for long-term immunosuppression is **administration** of **cyclosporin** , azathioprine and corticosteroids. Antibiotic prophylaxis is used to decrease the chance of infection with cytomegalovirus, Pneumocystis, Candida, Toxoplasma, and other opportunistic organisms. The major long-term complications include rejection, infection, hypertension, renal dysfunction, lipid abnormalities, and accelerated coronary atherosclerosis. This review provides an overview of the short- and long-term follow-up of the cardiac transplant recipient, including routine care as well as detection and management of the common complications.

May 1993 ,

3/3,K,AB/5 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.

0015244304 BIOSIS NO.: 200500151369

Mitochondrial permeability transition in CNS trauma: Cause or effect of neuronal cell death?

AUTHOR: Sullivan P G (Reprint); Rabchevsky A G; Waldmeier P C; Springer J E

AUTHOR ADDRESS: Spinal Cord and Brain Injury Res Ctr, Univ Kentucky, 240

HSRB, Lexington, KY, 40536, USA**USA

AUTHOR E-MAIL ADDRESS: PatSull@uky.edu

JOURNAL: Journal of Neuroscience Research 79 (1-2): p231-239 January 1, 2005 2005

MEDIUM: print

ISSN: 0360-4012 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Experimental traumatic brain injury (TBI) and spinal cord injury (SCI) result in a rapid and significant necrosis of neuronal tissue at the site of injury. In the ensuing hours and days, secondary injury exacerbates the primary damage, resulting in significant neurologic dysfunction. It is believed that alterations in excitatory amino acids (EAA), increased reactive oxygen species (ROS), and the disruption of Ca²⁺ homeostasis are major factors contributing to the ensuing neuropathology. Mitochondria serve as the powerhouse of the cell by maintaining ratios of ATP:ADP that thermodynamically favor the hydrolysis of ATP to ADP + Pi, yet a byproduct of this process is the generation of ROS. Proton-pumping by components of the electron transport system (ETS) generates a membrane potential (DELTAΨ_m) that can then be used to phosphorylate ADP or sequester Ca²⁺ out of the cytosol into the mitochondrial matrix. This allows mitochondria to act as cellular Ca²⁺ sinks and to be in phase with changes in cytosolic Ca²⁺ levels. Under extreme loads of Ca²⁺, however, opening of the mitochondrial permeability transition pore (mPTP) results in the extrusion of mitochondrial Ca²⁺ and other high- and low-molecular weight components. This catastrophic event discharges DELTAΨ_m and uncouples the ETS from ATP production. Cyclosporin A (CsA), a potent immunosuppressive drug, inhibits mitochondrial permeability transition (mPT) by binding to matrix **cyclophilin D** and blocking its binding to the adenine nucleotide translocator. Peripherally **administered** CsA attenuates mitochondrial dysfunction and neuronal damage in an experimental rodent model of TBI, in a dose-dependent manner. The underlying mechanism of neuroprotection afforded by CsA is most likely via interaction with the mPTP because the immunosuppressant FK506, which has no effect on the mPT, was not neuroprotective. When CsA was **administrated** after experimental SCI at the same dosage and regimen used TBI paradigms, however, it had no beneficial neuroprotective effects. This review takes a comprehensive and critical look at the evidence supporting the role for mPT in central nervous system (CNS) trauma and highlights the differential responses of CNS mitochondria to mPT induction and the implications this has for therapeutically targeting the mPT in TBI and SCI. Copyright 2004 Wiley-Liss. Inc.

...**ABSTRACT:** A (CsA), a potent immunosuppressive drug, inhibits mitochondrial permeability transition (mPT) by binding to matrix **cyclophilin D** and blocking its binding to the adenine nucleotide translocator. Peripherally **administered** CsA attenuates mitochondrial dysfunction and neuronal damage in an experimental rodent model of TBI,

```

? S CYCLOPHILIN(W) d
      6266  CYCLOPHILIN
      4958314  D
      S1      304  CYCLOPHILIN(W) D
? S INJECT? OR ADMINIST?
      1159690  INJECT?
      2331434  ADMINIST?
      S2 3151273  INJECT? OR ADMINIST?
? S S1 AND S2
      304  S1
      3151273  S2
      S3      14  S1 AND S2

```

? RD

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.

...completed examining records

S4 10 RD (unique items)

? S S4 AND PY<=1999

Processing

Processing

```

      10  S4
      37631536  PY<=1999
      S5      0  S4 AND PY<=1999

```

?

in...

...immunosuppressant FK506, which has no effect on the mPT, was not neuroprotective. When CsA was **administrated** after experimental SCI at the same dosage and regimen used TBI paradigms, however, it had...

? log off

```
31aug05 10:24:42 User231882 Session D1474.2
    $4.54      1.336 DialUnits File155
    $0.84    4 Type(s) in Format  4 (UDF)
    $0.84    4 Types
$5.38 Estimated cost File155
    $2.82      0.478 DialUnits File55
    $2.00    1 Type(s) in Format  5 (UDF)
    $2.00    1 Types
$4.82 Estimated cost File55
    $13.57     0.613 DialUnits File34
$13.57 Estimated cost File34
    $16.26     0.734 DialUnits File434
$16.26 Estimated cost File434
    $18.76     1.072 DialUnits File340
$18.76 Estimated cost File340
    OneSearch, 5 files,  4.234 DialUnits FileOS
    $1.33 TELNET
$60.12 Estimated cost this search
$60.25 Estimated total session cost  4.439 DialUnits
```

Logoff: level 05.06.01 D 10:24:42

You are now logged off